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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/715,285	11/17/2003	James Thompson	MBHB00-873-I (500.011)	5200

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EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/715,285	THOMPSON ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the communication filed 7-31-06.

Claims 16-24 are pending in the instant application.

Priority

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 09/103,636, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The newly amended claims recite the limitation of perfect complementarity between each strand of a double stranded nucleic acid molecule which targets a target RNA molecule. The claimed priority document, 09/103,636, of which the instant application is listed as a continuation in part, does not provide for the limitations now claimed.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

New Rejections Necessitated by Amendment

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 16-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fire et al and Zamore et al, the combination in view of McCall et al and Matulic-Adamic et al.

The claims are drawn to chemically synthesized siRNA molecules between 14-24 nucleotides in length, which strands within the siRNA comprise perfect complementarity, and which siRNA further comprise 5' and/or 3' caps, inverted nucleotides or deoxynucleotides and/or inverted abasic moieties, 2'O or 2'-F modifications, and one or more phosphorothioate internucleotide linkages, and which siRNA optionally targets

viral RNA or a mammalian target gene, and which composition further comprises a pharmaceutically acceptable diluent.

Fire et al (USPN 6,506,559) teach the advantages of targeting and inhibition of a target gene of known sequence using compositions comprising a pharmaceutically acceptable diluent and further comprising an siRNA molecule between 12-30 nucleobases in length compared to using other inhibitory oligonucleotide molecules such as antisense or ribozymes, which siRNA molecules comprise sequences sharing 100% homology with the complement of the target gene, and full complementarity between strands within the siRNA molecules (see the abstract; col. 7-11; claims 1-11).

Zamore et al (Cell, Vol. 101, pages 25-33, 2000) teach that 21-23 nucleobases are an optimal siRNA size range for the targeting and cleavage of mRNA in vitro (see esp. text and figures on pp. 27-32).

The primary references of Fire and Zamore do not teach siRNA molecules comprising 5' and/or 3' caps, inverted nucleotides or deoxynucleotides and/or inverted abasic moieties, 2'O or 2'-F modifications, and one or more phosphorothioate internucleotide linkages.

McCall et al (USPN 6,277,634) teach chemically synthesized double stranded nucleic acid molecules between 14-24 nucleotides comprising 5' and/or 3' caps comprising inverted (deoxy)abasic moieties, phosphorothioate internucleotide linkages, 2'-O-methyl or 2'-fluoro modified nucleotides, and a target region complementary to a viral or mammalian target gene, which nucleic acid molecule is in a pharmaceutically acceptable diluent (see entire document, esp. col. 5-6, 8-10 and 14).

Matulic-Adamic et al (USPN 5,998,203) teach chemically synthesized double stranded nucleic acid molecules between 14-24 nucleotides comprising 5' and/or 3' caps comprising inverted (deoxy)abasic moieties, phosphorothioate internucleotide linkages, 2'-O-methyl or 2'-fluoro modified nucleotides, and a target region complementary to a mammalian target gene, which nucleic acid molecule is in a pharmaceutically acceptable diluent (see entire document, esp. the abstract, col. 3-4, figures 8-10, 13, 18, col. 8-10, claims 1, 4-7, 9, 10, 16-39 and 41).

It would have been obvious to design and chemically synthesize siRNA molecules with fully complementary strands and between 14-24 nucleotides in length for the targeting and inhibition of expression of mammalian or viral target genes of known sequence because Fire teaches the advantages of using siRNA as inhibitory molecules and Zamore teaches the optimal size range for these inhibitory molecules to be between 21-23 nucleobases. One of ordinary skill in the art would have expected that siRNA molecules within this size range, and comprising perfect complementarity between strands within the siRNA molecule to be advantageous in inhibiting the expression of a known target gene in vitro because Fire teach the enhanced ability to inhibit expression of a target gene using siRNA compared to other inhibitory oligonucleotides including antisense and ribozymes.

It would have been obvious to one of ordinary skill in the art to incorporate the 5' and/or 3' caps comprising inverted (deoxy)abasic moieties, phosphorothioate internucleotide linkages, 2'-O-methyl or 2'-fluoro modified nucleotides modifications previously described by many and well known in the art because McCall and Matulic-

Adamic both teach the routine use and incorporation of such modifications for increasing polynucleotide and oligonucleotide stability. One of ordinary skill in the art would have been motivated to design siRNA with perfect complementarity between strands, and comprising target regions for mammalian or viral target genes because Fire and Zamore teach the use of siRNA molecules (including those with perfect complementarity) for target gene inhibition and McCall and Metalic-Adamic also teach the targeting and inhibition of mammalian or viral target genes using inhibitory oligonucleotides. One of ordinary skill in the art would have expected that the design and synthesis of siRNA molecules comprising the well known modifications including 5' and/or 3' caps comprising inverted (deoxy)abasic moieties, phosphorothioate internucleotide linkages, 2'-O-methyl or 2'-fluoro modified nucleotides would provide inhibitory molecules with enhanced stability and a longer biological half-life for a molecule provides for enhanced activity and resulting target gene inhibition. For these reasons, the instant invention would have been obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. ' 1.6(d)). The official fax telephone number for the Group is **571-273-8300**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on (571) 272-4517. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of

this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jane Zara
10-13-06